**Ketamine use: a review.** *Morgan CJA, Curran HV. Addiction 2011;364:2199-2207.*

This was a systematic review of the literature conducted for the Independent Scientific Committee on Drugs (ISCD). The findings were classified using David Nutt's 'rational scale' for assessing the harms of psychoactive substances. This matrix considers nine areas in three major domains: 'physical harms', 'dependence-related harms' and 'social harms'.

*Physical harms.* One of the most recently identified problems is the risk of ketamine-induced ulcerative cystitis. Another that has been documented is the occurrence of 'K-cramps' – episodes of intense abdominal pain as a result of prolonged, heavy ketamine use. The cause of this isn't clear but three small cases studies reported on young users who also had abnormal liver function and were found to have dilation of the common bile duct. All settled when ketamine was stopped. There is a significant risk of accidental death due to intoxication. Increased depression has been found in both daily and ex-ketamine users. There is evidence that ketamine can cause a resurgence of psychotic symptoms in schizophrenics but little evidence of any link between chronic, heavy use of ketamine and the diagnosis of a psychotic disorder. Infrequent recreational use of ketamine does not seem to be associated with cognitive impairment but frequent use does.

*Dependence-related harms domain.* Ketamine is most commonly snorted which leads to a rapid onset of effects and increases the abuse potential. There are some case reports of ketamine dependence and some evidence of compulsive behaviour. There is conflicting evidence about the existence of a withdrawal syndrome.

*Social harms.* As mentioned there is an increased risk of accidental injury – this is not highly surprising given ketamine is used as a dissociative anaesthetic and this can increase risk-taking behaviour. There is little data on other harms to the ketamine user within society and the cost to the health service. There are no data on human use of ketamine in pregnancy.

**Lower urinary tract changes in young adults using ketamine.** *Mak SK, Chan MTY, Bower WF, Yip SKH, Hou SSM, Wu BBB. The Journal of Urology 2011;186:610-614*

This study set out to investigate lower urinary tract changes in ketamine users in the community by establishing a mobile medical assessment service at youth centres in Hong Kong. They were able to identify the relative risks of dose, frequency of ingestion and duration of ketamine use and the lower urinary tract function was evaluated using the Pelvic Pain, Urgency and Frequency (PPUF) questionnaire, uroflowmetry and ultrasonography.

They found that the use of ketamine more than three times weekly was significantly associated with lower voided volumes. The PPUF questionnaire scores were significantly higher for ketamine use of more than 24 months. They also found that this normalised after about one year of abstinence.

**SMMGP comment:** Ketamine remains a relatively uncommon drug – only fourth favourite among clubbers and the British Crime Survey found it had been used by 1.7% of 16-24 year olds in the previous year. This places it below amphetamine and only just above magic mushrooms. However, there seems to have been a rise in recent years and the physical harms are becoming clearer.

Ketamine users with at least a two-year habit of three or more hits per week have altered bladder function that is symptomatic. The authors note that there is a high potential for confounding in the Hong Kong study – 80% of the population were using multiple drugs. It was also noted that around two-thirds of active ketamine users also consumed alcohol at the same time as ketamine. Problem ketamine users may present to services with other substance problems and they may certainly present

to primary care with no declaration of substance misuse problems at all but with bladder symptoms. The findings from these studies coalesce into a strong harm reduction message for ketamine users: regular use risks urinary tract health and physical harm from accidental injury as well as the potential damage to cognitive function.

**The increasing mortality burden of liver disease among opioid dependent people: cohort study.** *Gibson A, Randall D, Degenhardt A. Addiction 2011. Postprint. doi:10.1111/j.1360-0443.2011.03575.x*

This study looked at a cohort entering methadone treatment for heroin dependence (1980-85) in New South Wales, Australia. In total there were 2489 participants and 54,847 person-years of follow up. They linked data on the individuals with the Australian National Deaths Index to investigate any trends over time in mortality attributable to liver disease.

They worked out that there were 8.2 deaths per 1000 patient-years. Almost one in five (17%) deaths were from underlying liver-related causes, most commonly viral hepatitis. The overall mortality rate for any liver cause was 17 times greater than the general population but females fared much worse with a 28 times greater rate. Over time the trend was toward an increase in liver mortality and liver disease has now become the most common cause of mortality among opioid dependent people in this Australian cohort.

**Diagnosis of depression in former injection drug users with chronic hepatitis C.** *Scott JD, Wang CC, Coppel E, Lau A, Veitengruber J, Roy-Byrne P. Journal of Clinical Gastroenterology 2011; 45:462-467*

This study took 90 patients with chronic HCV as they wanted to find out how good two common depression screening questionnaires were in this group of patients. They used the Mini International Neuropsychiatric Interview administered by a psychiatrist as the 'gold standard'. They then got the participants to complete the Beck Depression Inventory (BDI) and Patient Health Questionnaire-9 (PHQ-9).

The BDI and PHQ-9 were both highly correlated with the gold standard. However, a PHQ-9 of ≥10 misclassified 52% of the patients. A PHQ-9 of ≥14 gave the best sensitivity (85.7%) and specificity (73.9%).

**SMMGP comment:** Liver disease is on its way up. This is partly because opioid dependent people are now living longer and this is allowing the relatively slow-developing liver disease to make its presence felt. It is highly likely the UK will be following the pattern of this Australian cohort and the emphasis in clinical practice needs to reflect this. As the authors point out there are more deaths from liver disease than there are from drug overdose and liver disease is both preventable and treatable.

The second study highlights an important area for primary care to develop. We need to develop the skills to give good support to those going through treatment for HCV. Depression has been reported as occurring in anything from 20 to 60% of people treated for HCV with ribavirin and interferon. PHQ-9 is a tool with which every GP in the country will be familiar. It's quick and it's easy. This study shows that PHQ-9 is a useful tool to screen before treatment but tends to over-diagnose depression.

SMMGP have now completed their role in putting together Part 1 of the new RCGP Certificate in the Detection, Diagnosis and Management of Hepatitis B and C in Primary Care. There are over 30 experienced trainers ready to deliver further local events and the next training days will be held in Birmingham on the 23rd September and Manchester on the 24th November. Please contact Marianne Thompson, Programme Coordinator, at the RCGP if you are interested in attending (hepbandc@rcgp.org.uk or call 0203 188 7653). The emodule is freely available at http://elearning.rcgp.org.uk but registration is needed first.

**Deaths of opiate/opioid misusers involving dihydrocodeine, UK, 1997-2007.** *Zamparutti G, Schifano F, Corkery JM, Oyefeso A, Ghodse AH. British Journal of Clinical Pharmacology 2011; 72:330-337*

This study analysed data voluntarily supplied by coroners. All cases pertaining to victims with a clear history of opiate/opioid misuse and in which dihydrocodeine (DHC), either on its own or in combination, was identified at post-mortem toxicology and/or implicated in death, were extracted from the database. The database used was the National Programme on Substance Abuse Deaths (np-SAD). The response rate from Coroners in England and Wales was as high as 95%.

In total there were 646 cases identified as DHC-related deaths. In 44% of cases it was directly implicated in the death and specifically mentioned. Complete information on prescribed medication was available in only 450 cases. In this group 45% had been regularly prescribed dihydrocodeine. DHC was identified in about 6.8% of all opiate/opioid related deaths held in the np-SAD database between 1997 and 2007.

**SMMGP comment:** There remains a limited amount of data on dihydrocodeine. The current Orange book guidelines suggest that dihydrocodeine might be an option in a few selected cases. However, the Orange guidelines pre-date the useful UK study, Leeds Evaluation of Efficacy of Detoxification Study (LEEDS), which suggested dihydrocodeine was less effective than buprenorphine for opiate detoxification. Overall, the evidence suggests dihydrocodeine is certainly no better and may well be worse.

The specific role of dihydrocodeine on drug deaths is less clear and the data from this study are limited. There is no denominator to assess the real risk from dihydrocodeine. We don't know, and this study doesn't speculate on, the actual number of dihydrocodeine scripts dispensed. This makes it challenging to draw firm conclusions. This study does reinforce some of the things we know already – polydrug use is dangerous. Over 96% of victims had polydrug intake with a mean of 3.30 substances found at post-mortem.

**The needle and the damage done: clinical and behavioural markers of severe femoral vein damage among groin injectors** *Senbanjo R, Strang J. Drug and Alcohol Dependence 2011, doi: 10.1016/j.drugalcdep.2011.06.001*

This was a short report that used a cohort study to identify the factors associated with severe femoral vein damage among groin injectors on oral opioid substitution treatment. The individuals were recruited through drug treatment centres in South East England. They investigated them with femoral ultrasonography and clinical grading of venous disease in each leg. They compared the 67 groin injectors with severely damaged femoral veins with 86 groin injectors with minimal or moderate damage.

The results showed that there were no significant differences between the groups in terms of age, gender or duration of injecting drug use. Severe femoral vein damage was associated with longer duration of groin injecting, use of thick needles (either blue hub 23G or green hub 21G), benzodiazepine injection, history of deep vein thrombosis and recurrent deep vein thrombosis, presence of depressed groin scar and chronic venous disease. The logistic regression analysis revealed that needle size and DVT were the main predictors of severe femoral vein damage.

**SMMGP comment:** There are some good practical points that can be pulled out of this study for clinicians (and policymakers) in primary care. Needle and syringe exchanges should consider only supplying appropriate lengths of orange-hub (25G) needles. It is obvious that early cessation of groin injecting would be helpful but avoidance of benzodiazepine injection and prompt diagnosis and treatment of DVT may also be useful.

The authors also suggest that routine examination of injecting sites among groin injecting patients should include an assessment of severity of venous disease in each leg. This may be something that GPs are less familiar with and this study graded

venous disease with the Clinical-Etiology-Anatomy-Pathophysiology (CEAP) classification. This is quite simple and grades on a scale from class 0 (no signs of venous disease) to class 6 (open venous ulcers). Early features are reticular veins (class 1) and varicose veins (class 2). The CEAP classification moves on to ankle oedema (class 3), then skin pigmentation in the gaiter area (class 4) and healed venous ulcers (class 5).

**Trends in substance abuse treatment 1998-2008: increasing older adult first-time admissions for illicit drugs.** *Arndt S, Clayton R, Schultz SK. American Journal of Geriatric Psychiatry 2011; 68:704-711*

The paper wanted to establish if the percentage of older adults entering substance misuse treatment for the first time was increasing. They looked at individuals who were having a first-time admission for a publicly funded substance abuse treatment in the United States. They measured demographic and other substance misuse variables at admission. They analysed data available over the period 1998 to 2008 and compared a group of young adults, aged 30-54 years, with those aged 55 years or older.

The results showed that the proportion of older adults going for substance abuse treatment for the first time is increasing relative to younger adults. The pattern of use is also changing with increasing illicit drug involvement (specifically cocaine and heroin) in older adult admissions. Cocaine was the most commonly mentioned drug. They showed that alcohol 'mentioned as a problem substance' was decreasing in both groups but slightly more rapidly in the older group. However, it remained the most important substance – mentioned in over 70% of the older age group as a problem substance and only slightly less in the younger group.

**SMMGP comment:** There seems little doubt now of the rising problem of the ageing drug user. The editorial talks about geriatric addictions and there are some key features of older users that need to be considered. This study shows that there are some subtle differences in substance misuse patterns in older people. In addition, there may be long-term chronic disease to manage and many of them may have lengthy histories of substance misuse with complications to address. Perhaps one of the greatest needs is for primary care and GPs to be more sensitive to the increasing risk in the population. Early detection is crucial.

**Heroin users' views and experiences of physical activity, sport and exercise.** *Neale J, Nettleton S, Pickering L. International Journal of Drug Policy 2011, doi: 10.1016/j.drugpo.2011.06.004*

This was a qualitative study that conducted in-depth interviews with 40 current or ex-heroin users. They then re-interviewed 37 of these participants three months later. The data presented in the paper are part of a larger qualitative study into recovery and they purposively recruited individuals who were starting a new episode of drug treatment or who had recently stopped using. Ten were beginning a new script for methadone or buprenorphine, ten were actively detoxing from illicit or prescribed opioids, ten had recently entered a residential rehabilitation service and ten had been free from all illicit or prescribed opioids for between 2 and 36 months.

They analysed the data to explore individuals' self-reported participation in physical activity, sport and exercise; their desire to participate; and any barriers to participation experienced. Firstly they reported on the physical activity and sport/exercise 'biographies' of the participants and the study showed that the participants were, in general, very interested in sport and exercise and were involved in a wide range of different active pastimes. They reported on their desire to participate and commented on how many really enjoyed being active. Many men and women stated that they would like to do more physical activity – both to try out new activities and resume activities they had done in the past. Finally, they explored some of the barriers to participation. One of the biggest was heavy drug use and few participants were able to play sport or take exercise during periods of heavy heroin use. Other barriers included factors such as poor health and feeling too tired or weak to exercise. Some felt too unfit and others didn't feel

confident about going to a public gym and some felt cautious about the addictive potential of exercise.

**SMMGP comment:** It's important to note that this study isn't looking at the effectiveness of physical activity or exercise programme interventions. However, as a qualitative study it is effective in challenging our attitudes towards those with opiate dependence and how they view exercise and physical activity.

They highlighted how many have do have relatively active levels – physical activity being defined as 'energy expenditure above resting level'. Walking and cycling as part of daily activities were common and the exercise value of them was well appreciated by many participants. Interestingly, the study highlights some of the barriers – social and structural – around the opportunities for sport and exercise. The study also noted how even local gyms can represent a formidable barrier to current and ex heroin users. Overall, the study suggested the important role of physical activity, sport and exercise in this group and that policies should reflect this.

**A short study to characterize use of Spice products (synthetic cannabinoids).** *Vandrey R, Dunn KE, Fry JA, Girling ER. Drug and Alcohol Dependence 2011. Available online ahead of print.*

This was an internet-based survey study conducted with adults reporting at least one lifetime use of a Spice product. Spice products are synthetic cannabinoids and are typical sold as 'herbal blends' or 'incense'. The authors point out that no controlled human experiments have been done on the effects of Spice products or the synthetic cannabinoids they contain.

They recruited participants via online message boards and forums. In total 168 participants met the eligibility criteria and completed the survey questions. The respondents were primarily Caucasian males. They reported on the subjective effects of Spice products and the positive effects included (with most common first): 'pleasant high', 'increased appetite', 'dream-like state', 'stimulated/energetic' and 'felt a floating feeling'.

Negative effects included: 'dry mouth', 'drowsy/tired', 'lightheaded', 'trouble remembering things', 'heart racing' and 'clumsiness'. Spice was reported as the drug of choice in just over one in five of the respondents and one in four reported no plans for future use of Spice.

**SMMGP comment:** These internet surveys are rough and ready – something the authors readily admit. They are likely to have significant bias in them in they way they recruit and the retrospective nature of them invites recall bias. However, they still provide some useful information into substances that may otherwise remain shrouded in anecdote. They can be constructed quickly and are going to be useful tools as further legal highs appear and legislation chases behind.

Spice products are not legal highs and are currently class B drugs in the UK – it's illegal to possess them, to give them away or to sell them. Unsurprisingly, they have largely cannabinoid type effects and this study helps to flesh out some of the positive and negative subjective experiences users are having.

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